IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	:	Jessie L.S.-Au, *et al*.
Serial No.	:	10/807,620
Filed:	:	March 24, 2004
For:	:	METHODS AND COMPOSITIONS TO DETERMINE THE CHEMOSENSITIZING DOSE OF SURAMIN USED IN COMBINATION THERAPY
TC/AU	:	1614
Examiner	:	James D. Anderson
Attorney Docket No.	:	TNI 2-011

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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Sir:

With respect to "print instructions", it is material error to ignore printed instructions in applying Section 103(a), even it the printed matter does not constitute patentable subject matter. *In re Gulack*, 217 USPQ 401 (Fed. Cir. 1983). More recently, the same Court stated that printed matter has patentable significance if there exists any new and unobvious functional relationship between the printed matter and the composition of the kit. *In re Ngai*, 35 USPQ2d 1384 (Fed. Cir. 2004). The MPEP expressly recognizes the vitality of the *Gulack* decision at MPEP § 2112.01 by stating, *inter alia*: "III. … [T]he critical question is whether there exists any new and unobvious functional relationship between the printed matter and the substrate."

The Examiner has stated that the instructions do not "breath 'life and meaning' into the claimed composition". The Examiner contends that, "One skilled in the art could readily administer any known therapeutic dose of suramin to treat cancer and does not require Applicant's instructions and nomogram to do so." This statement is absolutely false. In point of fact, administering a "therapeutic dose" of suramin will seriously injure the patient, as therapeutic doses of suramin are toxic. The whole point of the invention is to **NOT** administer a toxic dose of suramin to the patient. Rather, Applicants' teach and claim the determination of the suramin dose that would yield and maintain low and non-cytotoxic plasma concentrations of 90 µg/ml or less for the duration of presence of effective chemotherapy concentrations. This can **ONLY** be done using the dosing nomogram in claim 35. Contrary to the Examiner, one skilled in the art can only accomplish such maintenance of low and non-cytotoxic plasma

concentrations of suramin using the dosing nomogram in the claims. Without the dosing nomogram, the skilled artisan would just guess at a dose and likely would underdose the patient and not accomplish anything; or overdose and injure the patient. Hence, the nomogram surely breathes life and meaning into claim 35. Dr. Au's declarations of record further testify to this.

Briefly, Agyin discloses benzimidazole compounds, and proposes to use these in the treatment of cancer or viral diseases. Use in combination with cytotoxic agents and/or potentiators also is contemplated. None of Agyin's compounds have antitumor activity in animals bearing transplanted tumors. Agyin does not teach a suramin combination. Agyin does not teach using suramin as a potentiator. Agyin's benzimidazole compounds are not antimicrotubule compounds. Agyin does not teach using kits containing combinations of agents. Proof of these statements abounds in the record. See Applicants' July 1, 2009 response.

The combination of Tu, Klohs, *or* Lopez does not meet the claim limitations. Tu describes using suramin at doses that produced the maximum tolerated steady state plasma concentration of 150-200 µg/ml, maintained for up to 45 weeks, when combined with doxorubicin. Klohs, for example, calls for administration of suramin "at a dose which will produce plasma levels of about 100 to about 300 µg/ml." (Klohs @ col. 2, ll. 34-38). This is a cytotoxic dose of suramin. Hence, both Tu and Klohs are teaching the artisan to maintain the noted plasma levels (*viz*., 100 to 300 µg/ml) for an extended time period of, *e.g*., 12 to 16 weeks. Lopez teaches using suramin in a culture flask and does not teach the determination of the suramin dose in a subject. This combination, then, does not meet the claim limitations and, in particular, the dosing regimen in the dosing nomogram in claim 35.

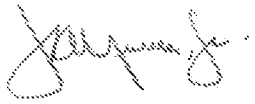
Inasmuch as neither Agyin, Tu, Klohs, or Lopez individually teach Applicants' dosing nomogram, nor even that a nomogram is necessary, nor even that low doses of suramin are needed, their combination by definition fails to meet the limitations of the claims.

The nomogram, then, has a new and unobvious functional relationship with the composition of the kit, and has patentable significance. Based on this patentable significance, the kit claims should be allowed.

Conclusion

Applicants respectfully request that the final rejection of the Examiner be reversed and that the claims be allowed and this application passed to issue.

Respectfully submitted,



Date: 06 August 2010

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